IN THE CLAIMS

Please cancel claims 1 to 37 and add the following new claims.

38. A method of screening for a substance which modulates phospho-specific binding of a fork-head associated (FHA) domain to a phosphopeptide, comprising:

(a) bringing a polypeptide comprising an FHA domain into contact with a phosphopeptide in the presence of one or more test substances;

(b) determining phospho-dependent binding of the FHA domain of said polypeptide to the phosphopeptide;

wherein the phosphopeptide is not Rad9p when the polypeptide comprising an FHA domain is Rad53p.

39. A method of screening according to claim 38 wherein said polypeptide comprising the FHA domain consists of the sequence;

$$\Psi\underline{G(R,K)}-[X_{10-40}]-\Psi\underline{(S,G)}(R,N)X\underline{(H,Q)}AX\Psi-[X_{10-50}]-$$
$$(S,T,G)NGTF\Psi(N,D)-[X_{8-25}]-(L,I)XXGDX\Psi X\Psi G$$

in which Ψ represents a hydrophobic amino acid, X represents any amino acid, and two or more residues which are separated by commas and are shown within brackets represent the possible residues which may be present at that position.

40. An assay method for identifying an FHA domain which has phospho-specific binding for a phosphopeptide of interest, or for determining the phospho-specific binding of an FHA domain to a phosphopeptide of interest comprising;

(a) bringing a polypeptide comprising a test FHA domain into contact with said phosphopeptide; and

(b) determining phospho-dependent binding of the test FHA domain of said polypeptide to the phosphopeptide;

wherein the polypeptide comprising the test FHA domain is not Rad53p.

41. An isolated polypeptide consisting of an FHA domain obtained by the method of claim 40, which binds to a phosphorylated polypeptide comprising the amino acid sequence -Thr(P)-X_1-X_2-Asp-, wherein Thr(P) denotes a phosphorylated threonine residue, and X_1 and X_2 each represent any amino acid residue and which consists of the sequence;

$$\Psi\underline{G(R,K)}-[X_{10-40}]-\Psi\underline{(S,G)}(R,N)X\underline{(H,Q)}AX\Psi-[X_{10-50}]-(S,T,G)NGTF\Psi(N,D)-[X_{8-25}]-(L,I)XXGDX\Psi X\Psi G$$

in which Ψ represents a hydrophobic amino acid, X represents any amino acid, and two or more residues which are separated by commas and are shown within brackets represent the possible residues which may be present at that position.

42. An assay method for identifying a phosphopeptide which

has phospho-dependent binding for an FHA domain, or for determining the phospho-specific binding of a phosphopeptide to an FHA domain comprising:

(a) bringing a test phosphopeptide into contact with a polypeptide comprising an FHA domain; and

(b) determining phospho-dependent binding of the test phosphopeptide to the FHA domain of said polypeptide;

wherein the phosphopeptide is not Rad9p.

43. A phosphopeptide obtained by a method according to claim 42 which binds to an FHA domain and which comprises the amino acid sequence of a peptide shown in Figure 2.

44. A phosphopeptide according to claim 43 which binds to the FHA1 domain of Rad53p and/or to Chk2.

45. An isolated nucleic acid molecule encoding a polypeptide according to claim 41 or the unphosphorylated form of a phosphopeptide according to claim 43 or claim 44.

46. A vector comprising a nucleic acid sequence according to claim 45 operably linked to one or more control sequences.

47. A host cell comprising a vector according to claim 46.

48. A transgenic non-human animal comprising a host cell according to claim 47.

49. A method according to claim 38, claim 40 or claim 41 wherein one or more of the phosphopeptide, FHA domain and test substance is in a test sample.

50. A method according to claim 49 comprising quantifying the amount of phosphopeptide, FHA domain or test substance in the sample.

51. A method according to claim 38, claim 40 or claim 41 further comprising purifying and/or isolating a test substance and/or substance of interest from a mixture or extract.

52. A method according to any one of claim 38, claim 40 and claim 41, comprising labelling one of said FHA domain and said phosphopeptide with a detectable label, immobilising the other of the FHA domain and the phosphopeptide on a solid support and bringing the FHA domain and the phosphopeptide into contact.

53. A method according to any one of claims claim 38, claim

40 and claim 41 wherein the end-point of the assay is phosphorylation of Rad53p protein.

54. A method of producing an phosphopeptide according to claim 43 or claim 44 comprising expressing nucleic acid encoding the unphosphorylated peptide and phosphorylating the expression product.

55. A substance which modulates the phospho-specific binding of an FHA domain to a target phosphopeptide and which comprises an antibody, single chain antibody or fragment thereof directed at the FHA domain at positions corresponding to Arg-70 and His-88 of Rad53p or directed at the motif -Thr(P)-X_1-X_2-Asp-, wherein Thr(P) denotes a phosphorylated threonine residue, and X_1 and X_2 each represent any amino acid residue.

56. A method of purifying a protein or polypeptide comprising an FHA domain able to bind a phosphopeptide in a phospho-specific manner, the method comprising contacting material comprising the polypeptide with a phosphopeptide, wherein the phosphopeptide is not Rad9p when the polypeptide comprising an FHA domain is Rad53p.

57. A method of purifying a phosphopeptide, the method comprising contacting material comprising the phosphopeptide with a protein or polypeptide comprising an FHA domain, wherein the phosphopeptide is not Rad9p when the polypeptide comprising an FHA domain is Rad53p.

58. A method of designing a mimetic of a phosphopeptide which has the biological activity of phospho-dependent binding to an FHA domain, or a method of designing a mimetic of an FHA domain which has biological activity of phospho-specific binding to a target phosphopeptide, said method comprising:

(a) analysing a substance having the biological activity to determine the amino acid residues essential and important for the activity to define a pharmacophore; and,

(b) modelling the pharmacophore to design and/or screen candidate mimetics having the biological activity, wherein the FHA domain is not the FHA2 domain of Rad53p.